REMARKS

This document is filed in reply to the Office Action dated November 21, 2005 ("Office Action").

Applicants have amended claim 1 to specify that the "acquiring and recording" step recited at lines 11-13 is carried out at the low magnification that the proceeding "scanning" step is conducted at. Support for the amendment appears in original claim 1 and at page 35, lines 18-20 of the specification. More specifically, original claim 1, at lines 7-13, recites steps of "scanning ... at a low magnification" and "acquiring and recoding a first image ... at [a] location." The specification, at page 35, lines 18-20, teaches that the these steps are carried out at the same low magnification. Applicants have also amended claim 1 to promote clarity. No new matter has been introduced.

Claims 1-29 are pending. Claims 8-16 and 20-28 have been withdrawn from further consideration for covering a non-elected invention. Claims 1-7, 17-19, and 29 are under examination. Reconsideration of this application is requested in view of the following remarks.

Rejection under 35 U.S.C. § 112, second paragraph

The Examiner rejected claims 1-7, 17-19, and 29 as being indefinite. See the Office Action, page 2, line 19 to page 3, line 6. Applicants respectfully traverse below.

Rejected claim 1 recites the following steps:

> obtaining a specimen field exposed to or labeled with at least a first fluorophore and a second fluorophore, the first fluorophore emitting photons at a first wavelength and the second fluorophore emitting photons at a second wavelength;
>
> exposing the specimen field to light sufficient to excite the first and second fluorophores;
>
> scanning the specimen field at a low magnification for first sources of photons at the first wavelength and for second sources of photons at the second wavelength;
>
> registering the location of each first source and each second source within the specimen field;
>
> acquiring and recording a first image of the specimen field at each location, the first image generated via an optical or electronic

filter that substantially blocks photons of the second wavelength but is permissive for photons of the first wavelength;

acquiring and recording a second image of the specimen field at each location at a high magnification, the second image generated via an optical or electronic filter that substantially blocks photons of the first wavelength but is permissive for photons of the second wavelength;

...

Referring to the obtaining step, the Examiner stated that "[i]t is not clear, what is being 'exposed to or labeled with' fluorophores: the 'specimen', or the 'specimen field'." See the Office Action, page 2, lines 19-20. Applicants note that the step at issue clearly recites "a specimen field exposed to or labeled with [fluorophores]." The specification also teaches the same. See, e.g., page 5, lines 27-30. Judging from the Examiner's statement, it appears to be his position that the phrase "specimen field" recited in this step should read "specimen," as recited in the preamble. Applicants would like to point out that a specimen field is just a field prepared from a specimen for fluorescence microcopy. See, e.g., the specification, page 15, lines 11-14 and page 16, lines 4-8. There is nothing indefinite about the obtaining step.

The Examiner also asserted that the location and magnification for the first acquiring and recording step recited in claim 1 are not clear. Applicants have amended claim 1 to promote clarity.

In view the above amendments and remarks, Applicants request that the rejection be withdrawn.

Rejection under 35 U.S.C. § 102(e)

The Examiner rejected claim 1 as being anticipated by Dunlay *et al.* US Patent 6,573,039 ("Dunlay"). See the Office Action, page 3, lines 21-22. Applicants respectfully traverse.

Claim 1, as amended, covers a method of detecting a target body in a specimen. The method includes acquiring and recording a first image and a second image at a location in a specimen field that has been exposed to a first fluorophore and a second fluorophore. The first

and second images are of two different fluorophores and acquired and recorded at two different magnifications, i.e., a low magnification and a high magnification.

According to the Examiner, "Dunlay describes use of two fluorescent labels to identify translocation a protein of interest (i.e., target body) from nucleus of a cell to cytoplasm." Referring to Examples 1 and 2 of Dunlay, the Examiner stated that

> A sample is loaded with two fluorescent labels, one - for [a] protein of interest, and another – to define individual cells. ... The sample is prescanned ... and fluorescent images of the two fluorescent labels are acquired. The image of the second fluorophore indicating location of the cell nucleus is used to calculate NetCyt Difference which is difference between cytoplasmic and nuclear fluorescent probes [i.e., the first fluorescent labels]...

See the Office Action, page 4, lines 4-15.

Dunlay does not teach acquiring an image at a low magnification at a first wavelength and at a high magnification at a second wavelength. In particular, Example 1 describes acquiring two images: (i) an image of a blue, DNA-specific fluorophore (DAPI), and (ii) an image of a transcription factor visualized by green-fluorophore labeled antibody. Both images are acquired at the same "20X magnification." See column 9, lines 31-45, FIG. 6, and FIGs. 8A-J. Indeed, "FIG. 6 is a representative display on a PC screen of data which was obtained in accordance with Example 1." See column 10, lines 32-33. Shown in the middle of the PC screen are two fluorescent images, "DAPI" and "Antibody." They clearly illustrate a nucleus staining image and a cytoplasm staining image of eight cells, both images being of the same apparent magnification.

As Dunlay teaches acquiring two images at a location of two different fluorophores at the same magnification, but not at two different magnifications as required in claim 1, it does not anticipate claim 1. Thus, Applicants request that the rejection be withdrawn.

Rejection under 35 U.S.C. § 103(a)

The Examiner rejected claims 1-7, 17-19, and 29 as being unpatentabe on two grounds. Applicants respectfully traverse each below.

I

The Examiner rejected claims 1-7, 17-19, and 29 as being obvious over Dunlay. The Examiner argued that it would have been obvious "to use the computer controlled optical system described in Dunlay for detection of 'any target body' of interest." See the Office Action, page 5, lines 3-4 and lines 10-14.

In contrast, Dunlay teaches acquiring two images at one location of two different fluorophores at the same magnification. It does not teach acquiring an image at a low magnification at a first wavelength and at a high magnification at a second wavelength. For at least this reason, Dunlay cannot render claim 1 obvious. Claims 2-7, 17-19, and 29 depend from claim 1, and are not obvious in view of Dunlay for at least the reason that claim 1 is not obvious in view of Dunlay.

As the Examiner stated, the Dunlay method involves calculating a NetCyt Difference. For this purpose, an image of a DNA-specific fluorophore, i.e., a nuclear image, is used as a "nuclear mask" to define two regions within a cell on an image of fluorophore-labeled antibody: (i) a region of a nucleus and (ii) a ring shaped region around the nucleus. The NetCyt Difference is calculated as the difference between the average fluoresce intensities of these two regions. See, FIGs. 8A-J and column 9, line 31 to column 10, line 7. In view of this teaching, one skilled in the art would recognize that the two images should be acquired at same magnification so as to obtain an accurate comparison. Thus, given Dunlay's focus on quantifying the fluoresce intensity difference, one skilled in the art would not have been motivated to alter Dunlay's method in order to acquire two images at one location of two fluorophores at two different magnifications, which is required in the method of claim 1, as well as claims 2-7, 17-19 and 29.

II

The Examiner rejected claims 1-7, 17-19, and 29 as being obvious over US Patent 4,581,334 to Kirchanski *et al.* ("Kirchanski") in view of Mason *et al.* ("Mason"). See the Office Action, page 6, lines 1-2.

Applicants respectfully traverse. Kirchanski teaches determining the phagocytic and killing ability of selected leukocyte subclasses based on two fluorescence signals obtained by

flow cytometry. See the abstract and column 1, lines 4-8. As correctly pointed out by the Examiner, this reference "does not teach acquiring fluorescent images." Mason, on the other hand, teaches fluorescent imaging methods. According to the Examiner, the combination of these two references renders claim 1 obvious.

Applicants note that, like Dunlay, Kirchanski and Mason, alone or combined, do not teach or suggest acquiring and recording two images at one location at two different magnifications as required in claim 1. Thus, for at least the same reasons stated in Part I above, Kirchanski and Mason, either alone or in combination, do not render claim 1 obvious. Claims 2-7, 17-19, and 29 depend from claim 1, and are not obvious over Kirchanski in view of Mason for at least the reasons that claim 1 is not obvious over the two references.

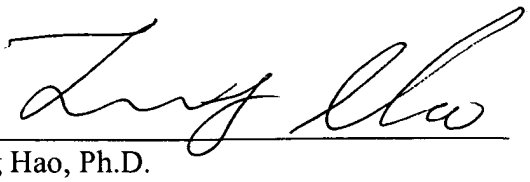
CONCLUSION

Applicants submit that grounds for the rejections asserted by the Examiner have been overcome, and that claims, as pending, define subject matter that is definite, novel, and non-obvious. On this basis, it is submitted that allowance of this application is proper, and early favorable action is solicited.

Please apply any other charges to deposit account 06-1050, referencing attorney docket 00530-097001.

Respectfully submitted,

Date: 2-21-2006



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